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24 Scientists, 14 Institutions Receive Funding for Collaborative Projects

Rhode Island Steps Up R&D Investment with Competitive Research Award Program Targeting Collaborative Efforts

(January 25, 2008)--The Rhode Island Science and Technology Advisory Council (STAC) today announced the awardees of the 2008 Collaborative Research Award program. The awards will provide support to nine projects, representing 24 scientists from 14 research organizations across Rhode Island.

The program is designed to advance research projects that are collaborative across institutions and well positioned to receive follow-on funding. Projects with significant technology development and commercialization potential are also encouraged.

Award recipients in 2008 include academic and industry scientists pursuing research in medicine, police forensics, engineering, chemistry, biology, oceanography and environmental science.

Awardees include:

- A collaboration to develop new ways to treat complicated pregnancies,

- Projects to discover better medicines for breast cancer, heart failure and asthma,
- The development of technologies that assist police in obtaining high quality evidence from low resolution video,
- The acquisition of shared equipment that enables Rhode Island scientists to better study proteins and their role in disease,
- An effort to better understand and manage green algae "blooms" in Narragansett Bay,
- The development of new platform for creating better hearing aid technology,
- A project to develop a fast and inexpensive test for anemia in at risk populations,
- And, an effort to accelerate the commercialization of novel genome sequencing technology and make Rhode Island a center of excellence in bioanalytics"

Winning teams include scientists from Bionica, Brown University, Celgen, NABsys, Organomed, ProThera Biologics, Rhode Island College, Women and Infants Hospital, Rhode Island Hospital, Rhode Island State Police, Roger Williams University, Salve Regina University and the University of Rhode Island.

To administer the program, STAC uses a competitive application process similar to that used by the National Science Foundation. Applications are evaluated by peer reviewers—scientific experts familiar with a proposal's area of focus—and a subcommittee of STAC members.

STAC has recommended that funding for the program be continued in 2009.

Program History

Investing in collaborative research is strategic for Rhode Island in two important ways. First, investment in collaborative research takes advantage of Rhode Island's unique ecosystem, one in which the state's compact geography and "tight knit" social networks enable collaborators to more easily share resources, equipment and information. Second, collaborative research is widely regarded as key to the multidisciplinary exploration emphasized by federal funding agencies and many commercial and foundation funding programs. Collaborative, multidisciplinary research also is considered to be a

successful route to novel intellectual capital and new company creation.

Through the Rhode Island Research Alliance STAC created a competitive, merit-based award program to support projects that are 1) of significant scientific merit; 2) collaborative across institutional boundaries; 3) catalytic in nature; and 4) well positioned to receive additional public and/or private funding. Projects with significant technology development and/or commercialization potential are also encouraged.

In 2007, STAC awarded nearly $1.5 million to eight teams of 32 scientists from 15 research institutions pursuing collaborative projects in medicine, engineering, chemistry, biology, oceanography and environmental science. The funding provided support for projects such as the development of high-tech toys to aid children with diseases such as cerebral palsy and the development of new marine-based drugs to fight a common and deadly hospital infection.

Evidence of the program's catalytic nature came in August 2007 when one funding recipient—a collaboration between Rhode Island College and Brown University—received a grant from the National Institutes of Health totaling $1.4 million to continue their pioneering testicular cancer research. This one award was almost equivalent to the amount of dollars the state invested in the program.

Forty-nine proposals were submitted for review during the 2008 cycle.

More About the Winners

Project 1: Increasing Success Rates for Complicated Pregnancies

This team is working to develop therapeutics that address dangerous pregnancy complications.

Collaborators:
Surendra Sharma, MD/PhD, Women and Infants Hospital
Yow-Pin Lim, MD/PhD, President and CEO, ProThera Biologics

Summary:

This team seeks to better understand the underlying mechanics of very dangerous pregnancy complications such as premature birth and intrauterine growth restriction (IUGR), a condition where a developing fetus is unable to achieve normal growth. These complications have been on the rise despite better clinical care and understanding.

This proposal will bring together the research groups at Women and Infants Hospital and ProThera Biologics to evaluate new therapies designed to treat these conditions, several of which are believed to be caused by an inflammatory response that injures or compromises the function of the placenta.

The team has been evaluated the cause of this inflammation and is making excellent progress in identifying specific proteins involved in the cascade of events that lead to preterm birth and IUGR. With the STAC award, the team will advance their study of potential therapeutics (in mice) in hopes of developing drugs that can be used to treat the condition in women. The team will also use the funds to continue their research on inflammation and pregnancy.

This unique alliance between an academic research laboratory at Women and Infants Hospital and a commercial research entity, ProThera Biologics, will create a multidisciplinary team to catalyze and synergize the technology development and commercialization of novel and promising anti-inflammatory agents with the ultimate goal of increasing success rates for complicated pregnancies. The data obtained from this collaborative study will be used to support a future translational study in humans and to prepare an application for federal funding.

Project 2: Creating a reliable, fast and affordable way to diagnose anemia.

This team seeks to explore non-invasive techniques for rapidly and reliably diagnosing anemia in at-risk communities.

Collaborators:
Dr. Gregory Crawford, Brown University
Dr. Gregory Jay, Rhode Island Hospital
Dr. Selim Suner, Rhode Island Hospital

Summary:
To quickly test for anemia, physicians often pull down the lower eyelid and examine the color of the inside lining of the eyelid, called the palpebral conjunctiva. This approach—quick and non-invasive—has been found to be inaccurate. However, the inside lining of the eyelid is an excellent place to *quantitatively* measure hemoglobin and other anemia-related blood components using spectroscopy. Spectroscopy measures how objects absorb and reflect light. All objects, including blood components, have unique color signatures when measured by a spectrometer. Spectrometer's can be engineered to be small and portable. Using this method, doctors can use a portable device to test for anemia by measuring things like how much hemoglobin is in a person's blood.

This Brown / Liefspan team will take what they have learned from initial studies, namely that spectrometry is a reliable way to test for anemia, and expand their work to develop a new device for this purpose. Using compact liquid crystal optical sensors, the team intends to develop and test an ultra-compact and inexpensive microchip spectrometer that can use a patient's eyelid to simply and quickly calculate hemoglobin concentration and reliably diagnose anemia.

To use the device health care workers only have to expose the lower eye lid and hold the sensor up to the exposed area to make a measurement. Thus, the device has the potential to be used by a wide array of healthcare providers in numerous environments.

Project 3: Acquisition of a state-of-the-art "isothermal titration calorimeter"

This project will enhance Rhode Island's research infrastructure by making a critical piece of equipment widely available to scientists studying proteins and their link to disease.

Collaborators:
Dr. Wolfgang Peti, Brown University
Dr. Bongsup Cho, University of Rhode Island

Summary:
Isothermal Titration Calorimetry (ITC) is the accepted standard for measuring what scientists call "biomolecular interactions." These are the foundational interactions in the human body, and include the interactions of proteins with each other (crucial for all life processes), the interaction of protein with DNA and the interaction of proteins with small molecules such as drugs.

Taking measurements of these interactions is vital to numerous areas of scientific investigation and especially valuable to the study of proteomics. The study of proteomics is central to understanding health and disease and vital to the development of new drug therapies.

The current instrumentation available to Rhode Island researchers for this measurement, a single instrument available in the NSF/EPSCoR Rhode Island Proteomics Core Facility, is outdated. Moreover, it has reached its experimental capacity because of too many users. Currently only five universities in the United States have access to this tool.

With this award, the Brown/URI partnership partners will install a new, state-of-the art ITC machine in the NSF/EPSCoR Rhode Island Proteomics Core Facility. The instrument, named the micro-volume Auto-iTC200, is widely regarded as the best of its kind. The instrument will strengthen Rhode Island's ability to support cutting-edge proteomics research.

This equipment will be available to all Rhode Island researchers and enhance the value of the state's shared core proteomics facility. The new instrument is two to four times faster than existing equipment, can be use in the high-throughput experiments essential to the study of proteins, has dramatically improved sample loading and cell cleaning capabilities (currently, the most frequent reason for failed experiments) and enables much more powerful data analysis and transfer. Most importantly, the instrument will substantially increase the number and types of ITC experiments that can be carried out by the RI research community.

Project 4: Making genome sequencing faster and less expensive

This award will support a partnership to accelerate the development of technology that makes genome sequencing faster and less expensive.

Collaborators:
Dr. John Oliver, NABSys, Inc.
Dr. Bernard Munge, Salve Regina University

Summary
The role that genetics plays in this country's most common and most lethal diseases is not well understood. To usher in an era of personalized, predictive, and preventive medicine, the ability to sequence human genomes at low cost, high speed, and high accuracy is required. The term "the $1,000 genome" has become shorthand for the promise of personalized medicine as enabled by a revolutionary sequencing technology.

NABsys Inc. is developing a sequencing technology called Hybridization-Assisted
Nanopore Sequencing (HANS) that will reduce the cost of sequencing a human genome to below $1000. The HANS method uses nanopores (nano-scale holes in silicon wafers) to sequence DNA and is expected to be significantly less expensive than other sequencing approaches. This award leverages the resources and expertise at NABsys Inc. and Salve Regina University, to take a step toward making the dream of the $1,000 genome a reality.

With this award, the partners will carry out a set of experiments that will provide data that significantly increases the likelihood of further funding of the NABsys Inc. sequencing technology. It is expected that the data will provide sufficient incentive for both federal agencies and venture firms to make further investments in the technology.

In addition to addressing an important medical need, the proposal addresses an area of high economic value. The DNA sequencing market is already at a respectable $1 billion per year.
A sequencing platform that has strong potential to sequence a human genome for less than $1,000 is of great interest to private funding sources such as venture capitalists and to government funding agencies.

The team also hopes to use their work to increase Rhode Island's research capacity in the area of bioanalytical technology. According to the Rhode Island Genomics and Sequencing Center, there is currently a single Applied Biosystems 3130xl sequencer in the state. This machine has the ability to produce approximately 100,000 bases of raw sequence or approximately 14,000 bases of finished sequence per day. A single NABsys machine would increase the state's sequencing capacity by over 10,000 fold. It would also mean that a significant percentage of the country's sequencing capacity would reside in Rhode Island.

A next-generation sequencing instrument in Rhode Island would significantly increase the state's bioanalytical capacity and place the state in a highly competitive position with respect to attracting future grant funding in areas requiring bioanalytical technology. A nanopore-based biosensing technology would be a significant asset for investigators doing research in disease areas in which the human genomes or microbial genomes are relevant (e.g. heart disease, cancer, stroke, diabetes, Alzheimer's, HIV, malaria), for forensics researchers. The technology would also be very useful for pathogen detection in the case of disease outbreaks or bioterrorist attacks

Project 5: Forensic Computer Vision: High quality evidence from low quality video

This collaboration between Brown University and the Rhode Island Police will use new computer visualization techniques to the extract high quality evidence from low quality video relevant to criminal investigations.

Collaborators:
Dr. Michael Black, Brown University
Lt. Dennis Pincince, Rhode Island State Police

Summary:
Crimes are captured on video every day, yet the quality of video images is often insufficient to yield actionable information for law enforcement. Recent advances in computer vision at Brown University are providing a new class of tools for extracting high quality images from low quality video. For example, Brown researchers have developed new methods for tracking people in video and using three dimensional modeling to estimate important biometric information such as height, weight, arm length,

etc.

This award will enable collaboration between Brown's Computer Science department and the Criminal identification Unit of the Rhode Island State Police. The collaboration is poised to establish Rhode Island as a leader in forensic video analysis.

The team will develop and test video analysis tools that will enable the police to recover 3D human motion in single camera scenarios, enable the 3D tracking of suspects in low-resolution video, employ new methods of reconstructing an image of a suspects face from low resolution video footage and provide biometric information about a suspect's height, weight and waist size.

Technology tested and developed in Rhode Island stands to serve as a national model for forensic video analysis.

Project 6: Understanding and better managing of "green tide" in Narragansett Bay, RI

This project seeks to develop create a deeper understanding of green tides so that these events can be better managed.

Collaborators:
Dr. Carol Thornber, University of Rhode Island
University of Rhode Island
Dr. Brian Wysor, Roger Williams University

Summary:
Green tides are prolific blooms of macroscopic green algae (i.e., seaweed). They are a persistent feature of shallow areas of Narragansett Bay from June-September every year, and while they have been observed for 100 years or more, these blooms appear to have increased in both size and duration over the past several decades.

Green tides can interfere with ecosystem processes, lead to environmental degradation, and negatively impact fishing and other recreational activities on the bay. This collaboration will seek to better understand green tides, the kinds of algae involved in the phenomena and ultimately develop better techniques from managing –and in some cases making productive use of--outbreaks.

Determining the species composition of algal blooms is of

critical importance. Given the severity of macroalgal blooms, a better ecological understanding of bloom dynamics is needed to foster informed management decisions. For example, if macroalgal blooms are to be controlled via biological methods in the future, understanding exactly *which* species contribute most to blooms is paramount.

This work will be the first attempt to elucidate patterns of diversity among green tides in Narragansett Bay (and the Northeastern U.S.) since the recognition of their increased frequency and duration in recent decades. A DNA barcoding strategy will be implemented to characterize diversity and minimize the problems of species identification in green algae. Specifically, the identity and geographic origin of species contributing to green tides will be evaluated using a newly developed DNA Barcode. In addition, studies of the natural history of bloom-impacted sites will be conducted to establish the extent, duration, timing and species composition of green tides throughout the bay. The work will result in a modern synthesis of the natural history of Narragansett Bay green tides and should help identify potential management strategies.

The barcode will facilitate studies of green tides elsewhere around the world. However, the real value of the designation of a green algal barcode is its general utility for diagnostic screening of biodiversity: this information could also be used to characterize ballast water for assessing biological pollution risks or for documenting native diversity for conservation initiatives.

The results of this project also are important to environmental management solutions that seek to utilize the biomass of green tide events. Green tide biomass may be useful as a heavy metal biosorbent, and, individually, numerous green tide species have been shown to produce compounds with a variety of desirable traits. Examples of such traits include compounds that are active against bloom-forming species, may represent an important nutritional supplement for humans or other organisms and show important medical applications (e.g., anti-cardiac, anti-inflammatory, and neuroprotective properties). This project will provide the means to unambiguously differentiate species whose compounds may represent commercially important product developments.

Project 7: Launching Rhode Island as the R & D Nexus for Next Generation Hearing Devices

Bionica Corporation is developing a state-of-the-art hearing aid to deliver optimal sound to patients suffering hearing loss. The primary objectives of this work are to evaluate the benefits of Bionica's system and move it from a hardware platform to testable hearing aid prototype.

Collaborators:
Kipp Bradford, Chief Technology Officer, Bionica
Dr. Laurie Heller, Brown University

Summary:
Bionica Corporation is developing a state-of-the-art hearing aid to deliver optimal sound to patients suffering hearing loss. The primary objectives of this work are to evaluate the stated benefits of Bionica's system and move it from a hardware platform to testable hearing aid prototype. The partnership will provide the acoustic research community with an advantage it has never had before: a system for the rapid deployment and real world evaluation of new processing algorithms to treat hearing loss.

Over 30 million people suffer from hearing loss in the United States. About two thirds of these people have mild hearing loss but do not use hearing aids. This population suffers an average of seven years before purchasing a hearing aid, struggling to hear in many situations or when there is significant background noise. About one tenth of the overall population tried hearing aids, but stopped using them after becoming dissatisfied with the performance and comfort of the devices. The remaining hard of hearing sufferers reluctantly continue to use hearings aids because they can't function without them.

The use of digital signal processor (DSP) in hearing aids brought exciting new features like noise reduction, feedback management, echo reduction, many channels of frequency tuning, and several settings for different environments. The acoustic signal processing algorithms running on a hearing aid DSP can be considered the "treatment" for hearing loss. However, the requirement for miniature size and minimal power consumption greatly constrained the possibility to provide novel treatments for

hearing loss, even with today's most advanced hearing aids. Further, the specialized electronics in existing hearing aids are incapable of maintaining the spatial separation of sounds, effectively eliminating important auditory cues essential for maximum intelligibility. As such, these devices only perform adequately as "near-field" amplifiers in low noise environments.

These limitations result in performance that falls far short of the proven capability of the signal processing algorithms developed for applications unconstrained by size and power.
The primary objectives of this work are to evaluate the stated benefits of the Clio system, and move it from a hardware platform to testable hearing aid prototype. Clio may benefit the hard of hearing community and the acoustic research community wherein until now, no system has existed for rapid deployment and real world evaluation of new processing algorithms to treat hearing loss.

Project 8: Improving breast cancer drugs

This research will identify new compounds to treat cancer that have similar efficacy with fewer side effects than current compounds such as tamoxifen, which has been successfully used as chemotherapy for multiple cancers, most notably breast cancer.

Collaborators:
Dr. John Williams, Rhode Island College
Dr. Matt Stoner, University of Rhode Island
Dr. Rebeka Merson, Rhode Island College
Dr. Karen Almeida, Rhode Island College
Dr. James N. Jacob, Organomed Corporation

Summary:
Molecules that target specific biological receptors can bind to them to produce therapeutic benefits. For example, in the treatment of cancer, chemotherapy drugs bind to tumors and shrink or eliminate the tumor.

In breast cancer treatment, drugs like Tamoxifen bind to a tumor to fight the disease. Knowledge of a receptor's

structure or of the molecular structure of successful drugs can inform the development of new ones.

This project will synthesize analogs of compounds that have been shown to be active at one or more of the estrogen receptors (the mechanism through which breast cancer is treated). The intention is to make new molecules that can be developed into drugs active against the disease and drugs that produce fewer of the significant side effects associated with current treatments.

Project 9: Developing New Drugs to Treat Congestive Heart Failure and Asthma

Collaborators:
Dr. Abraham Kovoor, University of Rhode Island
Dr. David Rowley, University of Rhode Island
Dr. Jeremy Celver, Chief Scientist, Celgen LLC
Dr. Bernard Munge, Salve Regina University

Project Summary
Congestive heart failure is the leading cause of death in the United States and the economic cost to the US in lost productivity and health-care expenses exceeds 20 billion dollars. Asthma, a chronic inflammation of the airways is another disease with high prevalence and social and economic costs.

Cellular proteins that play an important role in both heart disease and asthma are beta-adrenergic receptors (BAR). These receptors are targets of both anti-asthmatic drugs and drugs used to treat cardiovascular diseases.

Congestive heart failure is accompanied by decreased BAR function through a process that scientists call receptor desensitization. Similarly, therapies for asthma involve treatment with drugs that activate BAR to make breathing easier but with continued use, desensitization leads to drug tolerance, decreased asthma control, and increased risk of adverse cardiac events.

Drugs that address this desensitization could provide powerful treatments for people with both diseases. Partners on this project have found a promising lead and are working to capitalize on their discovery. Scientifically-diverse researchers from URI and Salve Regina will combine efforts

with the new Rhode Island biotechnology firm, CelGen, to identify this novel drug lead and to develop new tools for the rapid discovery and evaluation of additional therapies.

This award will catalyze the formation of this new collaboration and provide the means to develop proprietary technology for potential commercial development.

Next Steps

Rhode Island is especially well positioned to capitalize on research endeavors that build on current momentum and create stronger connections across the state's public and private research institutions.

STAC's Rhode Island Research Alliance is well positioned to continue this important work. A strong collaborative research alliance will create a powerful platform for consolidating limited resources towards a common agenda, maximizing the effect of the state's research investment, and strengthening Rhode Island's ability to compete for additional federal research dollars.

STAC recommends that Rhode Island's leadership support STAC's Research Alliance and its direct investment in collaborative research by renewing the Alliance's $1.5 million in funding in FY09.

The Research Alliance will again award these funds through a competitive review process to projects that are of significant scientific merit, highly collaborative across institutional boundaries, well positioned to secure additional funding, and have significant technology development and/or commercialization potential.